

Relevant to claim No.

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 CO7F9/58

C. DOCUMENTS CONSIDERED TO BE RELEVANT

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) IPC 7 CO7F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

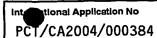
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BEILSTEIN Data, PAJ

Category • Citation of document, with indication, where appropriate, of the relevant passages

| Category | Citation of document, with indication, where appropriate, or the | riciovant to olditi tto: | | |
|---|--|---|--|--|
| Ρ,Χ | PHAM, VINH ET AL: "Design and Synthesis of Novel Pyridoxine 5'-Phosphonates as Potential Antiischemic Agents" JOURNAL OF MEDICINAL CHEMISTRY, vol. 46, no. 13, 14 August 2003 (2003-08-14), XP002287091 ISSN: 0022-2623 the whole document | | 1,4-9, 12,15, 17,18, 21,24, 30,31,44 | |
| X | COCKERILL, G. STUART ET AL: syntheses of building blocks for construction of phosphotyrosin PERKIN 1, no. 16, 2000, pages XP002287092 ISSN: 0300-922X compound 22c | for the ne mimetics" | 1,13 | |
| X Fur | ther documents are listed in the continuation of box C. | Patent family members are listed | in annex. | |
| considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or | | "T" later document published after the int or priority date and not in conflict with cited to understand the principle or the invention of particular relevance; the cannot be considered novel or cannot involve an inventive step when the discument of particular relevance; the cannot be considered to involve an indocument is combined with one or ments, such combination being obvict in the art. "&" document member of the same patent. | the claimed invention annot be considered to be document is taken alone the claimed invention an inventive step when the or more other such docuporous to a person skilled | |
| Date of the | e actual completion of the international search | Date of mailing of the international se | arch report | |
| | 13 July 2004 | 22/07/2004 | | |
| Name and | mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 | Authorized officer Elliott, A | | |

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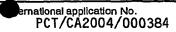
| | | PCT/CA2004/000384 | |
|--|---|---|--|
| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | | |
| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. | |
| Х | COCKERILL, STUART G. ET AL: "Facile syntheses of aryldifluorophosphonate building blocks" TETRAHEDRON LETTERS, vol. 40, no. 13, 26 March 1999 (1999-03-26), pages 2601-2604, XP004158095 ISSN: 0040-4039 compound 10 where Ar = 2-pyridyl | 1,13 | |
| X . | PATENT ABSTRACTS OF JAPAN vol. 017, no. 345 (C-1077), 30 June 1993 (1993-06-30) -& JP 05 043589 A (OTSUKA PHARMACEUT FACTORY INC), 23 February 1993 (1993-02-23) compounds 1, 5, 11 and 12 abstract | 1,13,24, 37,41,44 | |
| X | WO 01/64692 Al (MEDICURE INTERNATIONAL) 7 September 2001 (2001-09-07) cited in the application | 1,8-10, 14,15, 18,22, 24,28-44 | |
| | claims 1-60,120-180; examples 3,6,7,22 | | |
| X | WO 01/72309 A2 (MEDICURE INTERNATIONAL) 4 October 2001 (2001-10-04) | 1,8-10, 12,17, 18,22, 24, 29-32, 34,44 | |
| | claims 32-41,51-61.65.67; examples 3,6,7,22 | | |
| X | FRECHETTE, ROGER F. ET AL: "Novel hydroxyphosphonate inhibitors of CD-45 tyrosine phosphatase" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 7, no. 17, 9 September 1997 (1997-09-09), pages 2169-2172, XP004136407 ISSN: 0960-894X Table 1, entries 13-16 | 1,11-14, 22,24 | |
| X | BODUSZEK, BOGDAN: "The acidic cleavage of pyridylmethyl(amino)phosphonates. Formation of the corresponding amines" TETRAHEDRON, vol. 52, no. 38, 16 September 1996 (1996-09-16), pages 12483-12494, XP002287093 ISSN: 0040-4020 page 12490, compounds 17 - 22 | 1,8, | |

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Internal Application No PCT/CA2004/000384

| C.(Continu | ation) DOCUMENTS CONSIDERED TO BE RELEVANT | |
|------------|---|-----------------------|
| Category ° | Citation of document, with Indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | KONDO, KOICHI ET AL: "Synthesis of optically quadratic nonlinear phenylpyridylacetylenes" JOURNAL OF ORGANIC CHEMISTRY, vol. 57, no. 5, 28 February 1992 (1992-02-28), pages 1622-1625, XP002287094 ISSN: 0022-3263 compound 1 | 1,10,11 |
| X | EIDENHAMMER G ET AL: "Enzymes in organic chemistry, part 4: enantioselective hydrolysis of 1-acyloxy(aryl)methyl- and 1-acyloxy(heteroaryl)methylphosphonates with lipases from Aspergillus niger and Rhizopus oryzae. A comparative study" SYNTHESIS, no. 6, June 1996 (1996-06), pages 748-754, XP001182245 ISSN: 0039-7881 compounds 31 & 3m | 1,8,12 |
| X | PUDOVIK A N ET AL: "Synthesis of alkyl (3-pyridyl)hydroxymethylphosphonates and their IR spectra" RUSSIAN CHEMICAL BULLETIN, vol. 43, no. 9, September 1994 (1994-09), pages 1584-1586, XP009033070 ISSN: 1066-5285 compounds 1-4 | 1,8,12 |

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| Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet) |
|---|
| This international Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: |
| 1. X Claims Nos.: 1-21, 24-44 (all partially) because they relate to subject matter not required to be searched by this Authority, namely: |
| Although claims 28-42 are directed to methods of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compounds. |
| 2. X Claims Nos.: 1-21,24-44 (all partially) because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: |
| see FURTHER INFORMATION sheet PCT/ISA/210 |
| |
| 3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). |
| Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet) |
| This International Searching Authority found multiple Inventions in this international application, as follows: |
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| As all required additional search fees were timely paid by the applicant, this international Search Report covers all searchable claims. |
| 2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. |
| 3. As only some of the required additional search fees were timely paid by the applicant, this international Search Report covers only those claims for which fees were paid, specifically claims Nos.: |
| No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the Invention first mentioned in the claims; it is covered by claims Nos.: |
| 1000 1000 to the investigation in at the matter of the control of |
| Remark on Protest The additional search fees were accompanied by the applicant's protest. |
| No protest accompanied the payment of additional search fees. |

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 28-42 are directed to methods of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compounds.

Continuation of Box II.1

Claims Nos.: 1-21, 24-44 (all partially)

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box II.2

Claims Nos.: 1-21,24-44 (all partially)

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty of present claims 1-21 (the document referred to in paragraph '0003! of the application, W001/64692, is seen to disclose a number of novelty-destroying compounds – cf. the compounds prepared in Examples 3, 6, 7 and 22). Some statement as to the definite presence of a phosphonate substituent in the compounds of claim 1 is obviously missing as without such a statement, the claim encompasses pyridine (R1=R2=R3=R4=R5=H). So many documents were retrieved that it was impossible to determine which parts of the claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claims is impossible. Consequently, the search has been restricted to compounds clearly supported and disclosed by the application, i.e. to compounds seen as having the technical features of the exemplified compounds, namely compounds in which one of the stated phosphonate substituents is present and in which at least one of X and Y is either a hydroxy group or a fluoro group.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be

| | | The material Ap | Dication No. 1 O 17 CA2004 | 7000304 |
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| FURTHER INFORMATION CONTINUED FROM | PCT/ISA/ | 210 | | |
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formation on patent family members

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| PCT | CA2004/000384 | |

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|--|--|
| JP 05043589 A | 23-02-1993 | JP 2696150 B2 | 14-01-1998 |
| WO 0164692 A1 | 07-09-2001 | AU 3718501 A CA 2401655 A1 EP 1268498 A1 JP 2003525303 T US 2003114677 A1 US 2003120074 A1 US 2003181422 A1 US 2002010158 A1 | 12-09-2001 07-09-2001 02-01-2003 26-08-2003 19-06-2003 26-06-2003 25-09-2003 24-01-2002 |
| WO 0172309 A2 | 04-10-2001 | AU 4870301 A CA 2404329 A1 EP 1278526 A2 JP 2003528146 T US 2003114424 A1 US 2001056081 A1 | 08-10-2001 04-10-2001 29-01-2003 24-09-2003 19-06-2003 27-12-2001 |